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### Gene Mapping in Cattle

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## Gene Mapping in Cattle

Craig W. Beattie, Roger T. Stone, Michael D. Bishop, Sara L.F. Sunden, John W. Keele, and Steven M. Kappes<sup>1</sup>

Over the last decade, progress in molecular biologic techniques has brought the mapping of genes within the human and mouse genomes to a point where information on the location of groups of genes and additional anonymous, but unique, bits of DNA (markers) within their respective genomes can be brought to bear in developing a bovine genomic map. This is possible because of the conservation of genes, particularly those concerned with regulating important functions, between species into syntenic (single chromosome) groups.

Investment in the development of a bovine map is important for several reasons. While continued selection of desirable traits by the commercial livestock industry has made significant progress in improving moderately and highly heritable traits such as milk production, growth rate, and leanness, relatively little progress has been made in developing markers which significantly improve selection for less heritable traits or improve conception per service. Agribusiness research has also developed and provided diagnostic tests and vaccines for preventive herd health programs, yet little progress has been made in improving disease resistance while reducing costs.

To meet this challenge, genomic maps have been and are currently being developed in livestock in a number of university and commercial laboratories throughout the world. Although the development of maps for the genomes of a variety of livestock species per se will not provide additional technology for livestock improvement, they are essential for: a) providing "markers" for improved selection, and b) ultimately understanding how genes which regulate commercially important traits are expressed. Simply put, a bovine genomic map or genomic map for any economically important species is an essential starting point, not an end for development of the technology necessary to manipulate gene expression in livestock. The technological benefits and information derived from the human genome project make development of a bovine map easier. Without these benefits, mapping the genome of livestock would likely prove too expensive and long-term for the agricultural research system.

The Agricultural Research Service and others mapping, or planning to map, aspects of the bovine genome have objectives different from those of the human genome program. The initial objective in cattle is to develop and anchor 250-260 markers approximately equidistant along the genome; not to sequence the entire genome, but to provide markers for the selection of genes involved in regulating the expression of specific quantitative traits.

The two major components of the genome mapping program at the USDA-ARS MARC, Clay Center, NE are concerned with defining the location of map objects such as genes and anonymous DNA sequences and identifying which of those locations (markers) segregate to a significant extent with specific quantitative traits important to the live-

stock industry. Ultimately, identification of the locations or loci of genes which regulate quantitative traits (QTLs) such as marbling, meat quality, and disease resistance will allow rapid and improved selection of animals to improve these traits.

The initial objective of the genome mapping group at MARC is to simultaneously develop a genetic linkage and partial physical map of the bovine genome using identified markers. To develop a genetic linkage map, a group of anchor or index loci will serve as markers for any number of laboratories. Development of consensus index markers for similar loci is a primary focus of the genome group at MARC.

An interbreed-cross approach using families of cattle developed at MARC forms the basis for developing a genetic linkage map of the bovine genome. Since abundant polymorphisms (variations in form) within individual gene loci are generally not present within a species, a four-way cross reference population was designed to maximize this aspect of generating a map containing Type I anchor loci. Type I anchor (index) loci are evolutionarily conserved coding genes, the homologues of which are spaced at 15-25 centimorgan (CM; 15-25 million DNA bases) intervals in the human and mouse genome. The second type of linkage map takes advantage of Type II anchor loci which are species-specific DNA markers that exhibit a high degree of polymorphism. These loci include microsatellites or small repeats of particular DNA base pairs.

A physical map is based, in part, on localizing genes or known sequences of anonymous pieces of DNA directly onto an individual chromosome using a technique called *in situ* hybridization. Once identified these sites also serve as anchoring points for a map. The goal is to combine the physical and genetic linkage maps through the use of these anchor loci.

As the overall map is developed, the emphasis will shift and be expanded to include:

- a) identifying markers linked to traits of economic importance,
- b) characterizing selected genes at the cellular and molecular level, and
- c) using highly polymorphic genetic markers in marker assisted selection programs.

The potential dissection of quantitative traits in livestock currently refractory to genetic manipulation has substantial economic implications. They include the use of genetic markers in a marker-assisted selection index program, isolation of genes regulating commercially important traits, identification of genes responsible for undesirable traits, and improving biodiversity. The potential benefits of marker-assisted selection to the livestock producer simply in terms of cost benefit ratio from improved selection will have a proportional benefit to all livestock producers.

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